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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/513,962	02/08/2005	Ulf Forssmann	P67900US1	4706

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JACOBSON HOLMAN PLLC
400 SEVENTH STREET N.W.
SUITE 600
WASHINGTON, DC 20004

EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/513,962	FORSSMANN ET AL.	
	Examiner	Art Unit	
	Satyanarayana R. Gudibande	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *14-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/1205*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group II invention (claims 1-13) and election of R^1-CCL-14[10-74] where R^1 is bis-NNY belonging to SEQ ID NO: 12 as species in the reply filed on 7/9/07 is acknowledged.

Claims 1-18 are pending.

Claims 14-18 have been withdrawn from further consideration as being drawn to non-elected invention.

Claims 1-13 are examined on the merit.

Search for the elected species R^1-CCL-14[10-74] where R^1 is bis-NNY indicate that the species is free of art. Examiner extended the search and found art on R^1-CXCL12 [1-67] belonging to SEQ ID NO: 13 and has been applied in the rejections below.

Claim Objections

Claim 2 is objected to because of the following informalities: the word "compartment" on line 3 has been misspelled. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant application, applicants claim a method of inhibiting emigration of cells from intravascular compartment to tissues. Applicants also claim innumerable modifications to agonist molecules that inhibit the emigration of cells by receptor binding. Applicants also claim chemoattractant that is selected from the group consisting of a chemokine, a defensine, a leukotriene, a formyl-peptide or combinations thereof as well as mutants and/or variants of chemoattractant.

The MPEP clearly states that the purpose of the written description is to ensure that the inventor had possession of invention as of the filing date of the application, of the subject matter later claimed by him. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997). The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the application. These include, "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a

known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed invention is sufficient" MPEP 2163.

In the instant application, applicants claim a method of inhibiting the emigration of cells from the intravascular compartment into tissues (or through any membrane limiting any body compartment from another) by confronting the cells with an agonist specific for receptors involved with migration of said cells via a receptor thereby making the cell unresponsive to further activation.

The claims as recited claim innumerable modifications to agonist molecules that inhibit the emigration of cells by receptor binding comprising wherein R1 is a lipophilic, hydrophobic or polar aprotic residue, wherein R1 is any organic residue having up to 50 carbon atoms, which may be substituted by hetero atoms, and which organic residue is branched, unbranched, saturated, unsaturated or combinations thereof, R1 is an aromatic moiety, polyethylenoxid, moiety with 2 to 18 units, comprising residue and wherein R1 is any amino acid, or CH_3-$(CH_2)_n$-X; in which (CH_2)n is branched or unbranched X is -C (O) -NH-CH_2-C (O) -, -NHCH_2-C (O) -, -ONH-CH_2-C (O) -, -OCH_2-CH_2-C (O) -, -CH=CH-C (O) -, -C(O)-, or a covalent bond; and n is an integer of 1-17. The claims as recited and the specification as disclosed is inadequate in providing support for the claims as recited. The specification discloses only two modifications of the R1, and they are CRIC3, *n-nonanoyl-CCL14110-74]* and bis-NNY-*CCL14110-74], Bis-n-nonanoyl-CCL14110-74]*. The specification is vastly inadequate in supporting the claims as recited

wherein R1 is an aromatic moiety, a branched organic residue, etc. There are no core structures or partial structures of the agonist molecule with any of the proposed modifications as recited in the claims in the specification as originally presented.

The instant application claims chemoattractant that is selected from the group consisting of a chemokine, a defensine, a leukotriene, a formyl-peptide or combinations thereof as well as mutants and/or variants of chemoattractant. The specification on page 5 provide support for the conservative substitution of the amino acids in the chemoattractant and the specification is vastly silent on other types of variants and mutants such as addition, deletions, chemical modifications with the exception of the two modifications as discussed above.

Therefore, the claim(s) contains subject matter. which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 recite limitations such as "moiety with 2-18 units" and "comprising residue". It is unclear from the claim as recited the nature of the moiety that has 2-18 units. It is also unclear the meaning of "units" in the limitation. It is unclear the nature of the limitation "comprising residue".

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 recites a limitation, "$(CH_2)_n$ is branched or unbranched". The representation of "$(CH_2)_n$" only represents unbranched chain, for representing a branched chain, the representation includes $(CR^1R^2)_n$ in the formula wherein one of R^1 or R^2 is not hydrogen.

Therefore, claims 9 and 10 are being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 rejected under 35 U.S.C. 102(b) as being anticipated by US 6,140,064 issued to Loetscher, et al.

In the instant application, applicants claim a method of inhibiting the emigration of cells from the intravascular compartment into tissues (or through any membrane limiting any body compartment from another) by confronting the cells with an agonist specific for receptors involved with migration of said cells via a receptor thereby making the cell unresponsive to further activation.

Loetscher, et al., discloses a method of administering an agent that inhibits or promotes one or more function of a mammalian CXCR3 protein. In the method described, a compound that inhibits or promotes one or more function of human CXCR3 is administered to inhibit inflammation, as a result one or more inflammatory processes such as leukocyte emigration, chemotaxis or inflammatory mediator release is inhibited (column 28, lines 45-58). The chemokines are administered via a variety of routes including parenteral (e.g., intravenous, intra-arterial, etc.,) (column 30, lines 14-16) and inhibits emigration of leukocytes. The modulation of mammalian CXCR3 function is through inhibition or promotion of at least one function characteristic of a mammalian CXCR3 protein via selective inhibition or promotion of receptor-mediated function (column 28, lines 25-29). This meets the limitations of claim 1-5. The CXCR3 belongs to a subfamily of CXC chemokine (column 1, lines 32-33) and hence meets the limitation of clam 6.

Claims 1, 7-13 are rejected under 35 U.S.C. 102(b) as being anticipated by US WO 99/47158 of Clark-Lewis.

The reference of Clark-Lewis discloses the SEQ ID NO: 13 (RI-CXCLI2 [1-67]) of the instant application (SEQ ID NO: 6, page 2 of Sequence listing, also known as stromal derived factor one (SDF-1) in the cited reference). The cited reference of Clark-Lewis discloses C- and N-terminal modifications to the SDF-1 peptide (pages 19-28) that encompasses many of the modifications recited in claims 7-10 of the instant application. The reference also discloses the method of administration of the modified peptide in pharmaceutically acceptable carrier with a dosage regimen that is adjusted to provide optimum therapeutic response (page 16, lines 9-12 and line 31) for treating variety of autoimmune disease conditions and inflammation such as rheumatoid arthritis (page 11, line 15-21). This meets the limitations of claims 11-13. Since the reference discloses the elected species SEQ ID NO: 13 (RI-CXCLI2 [1-67]), it is inherent that the compound inhibits the emigration of cells from the intravascular compartment into tissues via interaction with the receptors on the cells making the cells unresponsive to further activation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were

made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over 6,140,064 issued to Loetscher, et al., as applied to claims 1-6 above, and further in view of WO 99/47158 of Clark-Lewis.

In the instant application, applicants claim a method of inhibiting the emigration of cells from the intravascular compartment into tissues (or through any membrane limiting any body compartment from another) by confronting the cells with an agonist specific for receptors involved with migration of said cells via a receptor thereby making the cell unresponsive to further activation. Applicants claim compound R1-CXCL12[1-67] and atopic dermatitis.

Loetscher, et al., discloses a method of administering an agent that inhibits or promotes one or more function of a mammalian CXCR3 protein. In the method described, a compound that inhibits or promotes one or more function of human CXCR3 is administered to inhibit inflammation, as a result one or more inflammatory processes such as leukocyte emigration, chemotaxis or inflammatory mediator release is inhibited (column 28, lines 45-58). The chemokines are administered via a variety of routes

including parenteral (e.g., intravenous, intra-arterial, etc.,) (column 30, lines 14-16) and inhibits emigration of leukocytes. The modulation of mammalian CXCR3 function is through inhibition or promotion of at least one function characteristic of a mammalian CXCR3 protein via selective inhibition or promotion of receptor-mediated function (column 28, lines 25-29). This meets the limitations of claim 1-5. The CXCR3 belongs to a subfamily of CXC chemokine (column 1, lines 32-33) and hence meets the limitation of clam 6.

The reference of Loetscher, et al., does not teach the chemokine species R1-CXCL12[1-67] belonging to SEQ ID NO: 13, nor the inflammation atopic dermatitis (AD).

The reference of Clark-Lewis discloses the SEQ ID NO: 13 (RI-CXCLI2 [1-67]) of the instant application (SEQ ID NO: 6, page 2 of Sequence listing, also known as stromal derived factor one (SDF-1) in the cited reference). The cited reference of Clark-Lewis discloses C- and N-terminal modifications to the SDF-1 peptide (pages 19-28) that encompasses many of the modifications recited in claims 7-10 of the instant application. The reference also discloses the method of administration of the modified peptide in pharmaceutically acceptable carrier with a dosage regimen that is adjusted to provide optimum therapeutic response (page 16, lines 9-12 and line 31) for treating variety of autoimmune disease conditions and inflammation such as rheumatoid arthritis (page 11, line 15-21). This meets the limitations of claims 11-13.

It would have been obvious to one of ordinary skill in the art to combine the teachings of Loetscher, et al., and Clark-Lewis, et al., to develop a method of inhibiting the emigration of cells from the intravascular compartment into tissues by confronting the cells with an agonist specific for receptors involved with migration of said cells via a receptor binding thereby making the cell unresponsive to further activation, because Loetscher, et al., teaches a compound that inhibits or promotes one or more function of human CXCR3 is administered to inhibit inflammation, as a result one or more inflammatory processes such as leukocyte emigration, chemotaxis or inflammatory mediator release is inhibited and Clark-Lewis teaches the compound RI-CXCLI2 [1-67] for the treatment autoimmune and inflammation disease conditions such as rheumatoid arthritis. One would have been motivated to do so given the fact that the compound that modulates human CXCR3 function inhibits the process of leukocyte emigration and RI-CXCLI2 [1-67] an antagonist of human chemokine receptor of class CXC chemokine is useful in treating inflammation such as rheumatoid arthritis. There would have been reasonable expectation of success given the fact the modified CXCLI2 [1-67] was shown to be useful in treating the autoimmune and inflammation disorders such as rheumatoid arthritis as shown by Clark-Lewis.

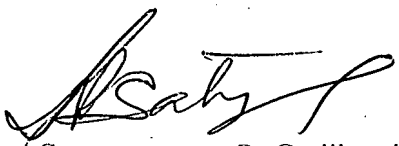
Therefore, the invention as a whole would have been prima facie obvious to one skilled in the art at the time invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Satyanarayana R. Gudibande, Ph.D.
Art Unit 1654